Evidence – Based Support for the Analgesic and Anti-Inflammatory Benefits of Ginger, Boswellia, Feverfew and Magnesium

Ginger Powder & Extract - Clinical Trials

Boswellia Serrata Extract – Clinical Trials

Feverfew - Mechanisms of Action and Clinical Efficacy for Migggbraine Prophylaxis

Magnesium - Anti-inflammatory and Analgesic Studies
Ginger Powder and Extract - Clinical Trials

- Comparison Between the Efficacy of Ginger and Sumatriptan in the Ablative Treatment of the Common Migraine.

- The Effect of Ginger for Relieving of Primary Dysmenorrhoea Effects of Ginger Extract on Knee Pain in Patients with Osteoarthritis.

- Anti-inflammatory Effects of Zingiber Officinale in Type 2 Diabetic Patients.

- The Effect of Ginger Powder Supplementation on Insulin Resistance and Glycemic Indices in Patients with Type 2 Diabetes: A Randomized, Double-Blind, Placebo-Controlled Trial

- The Effects of Ginger Consumption on Glycemic Status, Lipid Profile and Some Inflammatory Markers in Patients with Type 2 Diabetes Mellitus.

- A Review of the Gastroprotective Effects of Ginger (Zingiber Officinal Roscoe) Comparative Efficacy and Tolerability of 5-Loxin and Aflapin Against Osteoarthritis of the Knee: A Double Blind, Randomized, Placebo Controlled Clinical Study.
GINGER POWDER AND EXTRACT
CLINICAL TRIALS

Comparison between the efficacy of ginger and sumatriptan in the ablative treatment of the common migraine.

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Abstract

Frequency and torment caused by migraines direct patients toward a variety of remedies. Few studies to date have proposed ginger derivates for migraine relief. This study aims to evaluate the efficacy of ginger in the ablation of common migraine attack in comparison to sumatriptan therapy. In this double-blinded randomized clinical trial, 100 patients who had acute migraine without aura were randomly allocated to receive either ginger powder or sumatriptan. Time of headache onset, its severity, time interval from headache beginning to taking drug and patient self-estimation about response for five subsequent migraine attacks were recorded by patients. Patients' satisfaction from treatment efficacy and their willingness to continue it was also evaluated after 1 month following intervention. Two hours after using either drug, mean headaches severity decreased significantly. Efficacy of ginger powder and sumatriptan was similar. Clinical adverse effects of ginger powder were less than sumatriptan. Patients' satisfaction and willingness to continue did not differ. The effectiveness of ginger powder in the treatment of common migraine attacks is statistically comparable to sumatriptan. Ginger also poses a better side effect profile than sumatriptan.
The effect of ginger for relieving of primary dysmenorrhoea.

Jenabi E., J Pak Med Assoc. 2013 Jan;63(1):8-10
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Abstract

OBJECTIVE:
To assess the effectiveness of ginger in providing relief to patients of primary dysmenorrhoea.

METHODS:
The clinical trial was conducted at Toyserkan Azad University in western Iran from July 10 to September 5, 2010. It comprised of 70 female students of the university with primary dysmenorrhoea. The subjects were randomly divided into two equal groups and were given either placebo or ginger in capsule form for 3 days in first menstruation cycles. They graded the severity of their pain using a visual analogue scale. A 5-point Likert scale was used to assess response to treatment. Wilcoxon's rank-sum test was used to compare the severity of pain in the two groups.

RESULTS:
Compared with the baseline, the decrease in the visual analogue scores of post-therapy pain in the ginger group was significantly greater than that for placebo group. In the ginger group, 29 (82.85%) subjects reported an improvement in nausea symptoms, compared with 16 (47.05%) in the placebo group.

CONCLUSION:
Ginger is effective in minimising the pain severity in primary dysmenorrhoea.
The effect of ginger consumption on glycemic status, lipid profile and some inflammatory markers in patients with type 2 diabetes mellitus.

Arablou T¹, Aryaeian N, Valizadeh M, Sharifi F, Hosseini A, Djalali M.

Abstract

Abstract Objective: To assess the effect of ginger consumption on glycemic status, lipid profile and some inflammatory markers in patients with type 2 diabetes mellitus. Methods: In a double-blinded, placebo-controlled clinical trial, 70 type 2 diabetic patients were enrolled. They allocated randomly into ginger group and control group. They consumed 1600 mg ginger versus 1600 mg wheat flour placebo daily for 12 weeks. Serum sugar, lipids, CRP, PGE2 and TNFα were measured before and after intervention. Results: Ginger reduced fasting plasma glucose, HbA₁C, insulin, HOMA, triglyceride, total cholesterol, CRP and PGE2 significantly compared with placebo group (p < 0.05). There were no significant differences in HDL, LDL and TNFα between two groups (p > 0.05). Conclusion: Ginger improved insulin sensitivity and some fractions of lipid profile, and reduced CRP and PGE2 in type 2 diabetic patients. Therefore ginger can be considered as an effective treatment for prevention of diabetes complications.
Anti-inflammatory effects of zingiber officinale in type 2 diabetic patients.


Abstract

Purpose: Low-grade inflammation, a common feature in type 2 diabetes (DM2), causes some chronic complications in these patients. The present study was aimed to evaluate the effects of ginger (Zingiber officinale) on pro-inflammatory cytokines (IL-6 and TNF-α) and the acute phase protein hs-CRP in DM2 patients as a randomized double-blind placebo controlled trial. Methods: A total of 64 DM2 patients randomly were assigned to ginger or placebo groups and received 2 tablets/day of each for 2 months. The concentrations of IL-6, TNF-α and hs-CRP in blood samples were analyzed before and after the intervention. Results: Ginger supplementation significantly reduced the levels of TNF-α (P = 0.006), IL-6 (P = 0.02) and hs-CRP (P = 0.012) in ginger group in comparison to baseline. Moreover, the analysis of covariance showed that the group received ginger supplementation significantly lowered TNF-α (15.3 ± 4.6 vs. 19.6 ± 5.2; P = 0.005) and hs-CRP (2.42 ± 1.7 vs. 2.56 ± 2.18; P = .016) concentrations in comparison to control group. While there were no significant changes in IL-6 (7.9 ± 2.1 vs. 7.8 ± 2.9; P > .05). Conclusion: In conclusion, ginger supplementation in oral administration reduced inflammation in type 2 diabetic patients. So it may be a good remedy to diminish the risk of some chronic complications of diabetes.
The effect of ginger powder supplementation on insulin resistance and glycemic indices in patients with type 2 diabetes: A randomized, double-blind, placebo-controlled trial.


Abstract

OBJECTIVE:
To identify the effect of some herbal products on insulin resistance. Regarding the scientific evidences existing about ginger, this research was therefore carried out to identify the effect of ginger supplementation on insulin resistance and glycemic indices in diabetes mellitus.

METHODS:
This is a randomized, double-blind, placebo-controlled trial in which 88 participants affected by diabetes were randomly assigned into ginger (GG) and placebo (PG) groups. The GG received 3 one-gram capsules containing ginger powder whereas the PG received 3 one-gram microcrystalline-containing capsules daily for 8 weeks. HbA1c, fructosamine, fasting blood sugar (FBS), fasting insulin, homeostasis model assessment insulin resistance index (HOMA-IR), β-cell function (β%), insulin sensitivity (S%) and the quantitative insulin sensitivity check index (QUICKI) were assessed before and after the intervention.

RESULTS:
FBS mean showed a decrease of 10.5% (p=0.003) in the GG whereas the mean had an increase of 21% in the PG (p=0.01). Variation in HbA1c mean was in line with that of FBS. Statistical difference was found in the two groups before and after the intervention in terms of median of fasting insulin level, S% and HOMA-IR (P<0.005). Moreover QUICKI mean increased significantly in the two groups, the mean difference, however, was significantly higher in the GG.

CONCLUSIONS:
The study demonstrated that daily consumption of 3 one-gram capsules of ginger powder for 8 weeks is useful for patients with type 2 diabetes due to FBS and HbA1c reduction and improvement of insulin resistance indices such as QUICKI index.
A review of the gastroprotective effects of ginger (Zingiber Officinale Roscoe).


Abstract
The rhizomes of Zingiber officinale Roscoe (Zingiberaceae), commonly known as ginger is an important kitchen spice and also possess a myriad health benefits. The rhizomes have been used since antiquity in the various traditional systems of medicine to treat arthritis, rheumatism, sprains, muscular aches, pains, sore throats, cramps, hypertension, dementia, fever, infectious diseases, catarrh, nervous diseases, gingivitis, toothache, asthma, stroke and diabetes. Ginger is also used as home remedy and is of immense value in treating various gastric ailments like constipation, dyspepsia, belching, bloating, gastritis, epigastric discomfort, gastric ulcerations, indigestion, nausea and vomiting and scientific studies have validated the ethnomedicinal uses. Ginger is also shown to be effective in preventing gastric ulcers induced by nonsteroidal anti-inflammatory drugs [NSAIDs like indomethacin, aspirin], reserpine, ethanol, stress (hypothermic and swimming), acetic acid and Helicobacter pylori-induced gastric ulcerations in laboratory animals. Various preclinical and clinical studies have also shown ginger to possess anti-emetic effects against different emetogenic stimuli. However, conflicting reports especially in the prevention of chemotherapy-induced nausea and vomiting and motion sickness prevent us from drawing any firm conclusion on its effectiveness as a broad spectrum anti-emetic. Ginger has been shown to possess free radical scavenging, antioxidant; inhibition of lipid peroxidation and that these properties might have contributed to the observed gastroprotective effects. This review summarizes the various gastroprotective effects of ginger and also emphasizes on aspects that warrant future research to establish its activity and utility as a gastroprotective agent in humans.
Boswellia Serrata Extract – Clinical Trials

• Comparative Efficacy and Tolerability of 5-Loxin and Aflapin Against Osteoarthritis of the Knee. A Double Blind, Randomized, Placebo Controlled Clinical Study.

• Long-term Efficacy of Boswellia Serrata in Four Patients with Chronic Cluster Headache

• Efficacy and Tolerability of Boswellia Serrata Extract in Treatment of Osteoarthritis of Knee—a Randomized Double Blind Placebo Controlled Trial.

• Effect of Boswellia serrata Supplementation on Blood Lipid, Hepatic Enzymes and Fructosamine Levels in Type 2 diabetic Patients
BOSWELLIA SERRATA EXTRACT
CLINICAL TRIALS

Comparative efficacy and tolerability of 5-Loxin\textsuperscript{®} and Aflapin\textsuperscript{®} against osteoarthritis of the knee: A double blind, randomized, placebo controlled clinical study.

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Abstract
Aflapin\textsuperscript{®} is a novel synergistic composition derived from \textit{Boswellia serrata} gum resin (Indian Patent Application No. 2229/CHE/2008). Aflapin is significantly better as an anti-inflammatory agent compared to the \textit{Boswellia} extracts presently available in the market. A 90-day, double-blind, randomized, placebo-controlled study was conducted to evaluate the comparative efficacy and tolerability of 5-Loxin\textsuperscript{®} and Aflapin\textsuperscript{®} in the treatment of osteoarthritis (OA) of the knee (Clinical trial registration number: ISRCTN80793440). Sixty OA subjects were included in the study. The subjects received either 100 mg (n=20) of 5-Loxin\textsuperscript{®} or 100 mg (n=20) of Aflapin\textsuperscript{®} or a placebo (n=20) daily for 90 days. Each patient was evaluated for pain and physical functions by using the standard tools (visual analog scale, Lequesne's Functional Index, and Western Ontario and McMaster Universities Osteoarthritis Index) at the baseline (day 0), and at days 7, 30, 60 and 90.
A battery of biochemical parameters in serum, urine and hematological parameters in citrated whole blood were performed to assess the safety of 5-Loxin® and Aflapin® in OA subjects. Fifty seven subjects completed the study. At the end of the study, both 5-Loxin® and Aflapin conferred clinically and statistically significant improvements in pain scores and physical function scores in OA subjects. Interestingly, significant improvements in pain score and functional ability were recorded as early as 7 days after initiation of the study in the treatment group supplemented with 100 mg Aflapin. Corroborating the improvements in pain scores in treatment groups, our in vitro studies provide evidences that Aflapin® is capable of inhibiting cartilage degrading enzyme MMP-3 and has the potential to regulate the inflammatory response by inhibiting ICAM-1. Aflapin® and 5-Loxin® reduce pain and improve physical functions significantly in OA subjects. Aflapin exhibited better efficacy compared to 5-Loxin®. In comparison with placebo, the safety parameters were almost unchanged in the treatment groups. Hence both 5-Loxin® and Aflapin® are safe for human consumption.

In summary, the present study provides the evidence in support of the potential efficacy and tolerability of 5-Loxin® and Aflapin® in subjects with OA; 5-Loxin® and Aflapin significantly improved joint function. Aflapin exhibited better therapeutic efficacy over 5-Loxin® at 100 mg/day; it reduces pain rapidly, as early as after 1 week of treatment. Furthermore, in vitro studies also provide evidences that compared to 5-Loxin, Aflapin is capable of inhibiting cartilage degrading enzyme MMP-3 and has the potential to regulate the inflammatory component in by inhibiting ICAM-1. Most importantly, we have observed that 5-Loxin® and Aflapin® are safe for human consumption, even for long term supplementation. 5-Loxin® and Aflapin® are promising alternative therapeutic options, that may be used as nutritional supplements for management of OA.
Long-term efficacy of Boswellia serrata in four patients with chronic cluster headache.

Lampi C1, Haider B, Schweiger C.

Abstract

BACKGROUND:
Cluster headache is an extremely severe and debilitating trigemino-autonomic pain syndrome. About 10% of patients with cluster headache manifest a chronic form (CCH). The present case series study aims to evaluate the long-term efficacy of Boswellia serrata (Sallaki H15) on headaches and disturbed sleep in patients with CCH.

CASE RESULTS:
In an open-label study, four patients with CCH and disturbed sleep received oral B. serrata.

CONCLUSION:
The results provide Class IV evidence that oral B. serrata reduces the intensity and frequency of headaches in patients with CCH.
Efficacy and tolerability of Boswellia serrata extract in treatment of osteoarthritis of knee—a randomized double blind placebo controlled trial.


Abstract

Osteoarthritis is a common, chronic, progressive, skeletal, degenerative disorder, which commonly affects the knee joint. Boswellia serrata tree is commonly found in India. The therapeutic value of its gum (guggulu) has been known. It posses good anti-inflammatory, anti-arthritis and analgesic activity. A randomized double blind placebo controlled crossover study was conducted to assess the efficacy, safety and tolerability of Boswellia serrata Extract (BSE) in 30 patients of osteoarthritis of knee, 15 each receiving active drug or placebo for eight weeks. After the first intervention, washout was given and then the groups were crossed over to receive the opposite intervention for eight weeks. All patients receiving drug treatment reported decrease in knee pain, increased knee flexion and increased walking distance. The frequency of swelling in the knee joint was decreased. Radiologically there was no change. The observed differences between drug treated and placebo being statistically significant, are clinically relevant. BSE was well tolerated by the subjects except for minor gastrointestinal ADRs. BSE is recommended in the patients of osteoarthritis of the knee with possible therapeutic use in other arthritis.
Effect of Boswellia serrata supplementation on blood lipid, hepatic enzymes and fructosamine levels in type 2 diabetic patients.


Abstract

BACKGROUND:
Type 2 diabetes is an endocrine disorder that affects a large percentage of patients. High blood glucose causes fatty deposits in the liver which is likely to increase in SGOT and SGPT activities. Significant increase in SGOT/SGPT and low HDL levels is observed in patients with diabetes. Serum fructosamine concentration reflects the degree of blood glucose control in diabetic patients. This study was aimed to investigate the antidiabetic, hypolipidemic and hepatoprotective effects of supplementation of Boswellia serrata in type 2 diabetic patients.

METHODS:
60 type 2 diabetic patients from both sexes (30 males and 30 females) were dedicated to the control and intervention groups (30 subjects per group). Boswellia serrata gum resin in amount of 900 mg daily for 6 weeks were orally administered (as three 300 mg doses) in intervention group and the control group did not receive anything. Blood samples were taken at the beginning of the study and after 6 weeks. Blood levels of fructosamine, lipid profiles as well as hepatic enzyme in type 2 diabetic patients were measured

RESULTS:
Treatment of diabetic patient with Boswellia serrata was caused to significant increase in blood HDL levels as well as a remarkable decrease in cholesterol, LDL, fructosamine (p < 0.05) SGPT and SGOT levels after 6 weeks (p < 0.01). In spite of reduction of serum triglyceride, VLDL levels in intervention group, we did not detect a significant difference after 6 weeks.

CONCLUSION:
This study showed that Boswellia serrata supplementation can be beneficial in controlling blood parameters in patients with type 2 diabetes. Therefore, its use can be useful in patients with medicines.
Feverfew: Mechanisms of Action and Clinical Efficacy for Migraine Prophylaxis

- Randomised Double-Blind Placebo-Controlled Trial of Feverfew in Migraine Prevention

- Efficacy of Feverfew as Prophylactic Treatment of Migraine

- The Therapeutic Activity of Feverfew on Migraines and Epilepsy May be Due to Its GABA-Benzodiazepine Modulatory Effects.—Green Med Info Summary

- The Efficacy and Safety of Feverfew (Tanacetum Parthenium L.): An Update of a Systematic Review

- Gene Responses of Human Monocytic Cells for the Detection of Anti-migraine Activity of Fever Extracts

- Application of NFkappaB Inhibitor for Arthritis

- Inhibition of 5-Lipoxygenase and Cyclo-Oxygenase in Leukocytes by Feverfew. Involvement of Sesquiterpene Lactones and Other Components
Feverfew - Mechanisms of Action and Clinical Efficacy for Migraine Prophylaxis

Randomised double-blind placebo-controlled trial of feverfew in migraine prevention.


Abstract

The use of feverfew (Tanacetum parthenium) for migraine prophylaxis was assessed in a randomised, double-blind, placebo-controlled crossover study. After a one-month single-blind placebo run-in, 72 volunteers were randomly allocated to receive either one capsule of dried feverfew leaves a day or matching placebo for four months and then transferred to the other treatment limb for a further four months. Frequency and severity of attacks were determined from diary cards which were issued every two months; efficacy of each treatment was also assessed by visual analogue scores. 60 patients completed the study and full information was available in 59. Treatment with feverfew was associated with a reduction in the mean number and severity of attacks in each two-month period, and in the degree of vomiting; duration of individual attacks was unaltered. Visual analogue scores also indicated a significant improvement with feverfew. There were no serious side-effects.
Efficacy of feverfew as prophylactic treatment of migraine.


Abstract

Seventeen patients who ate fresh leaves of feverfew daily as prophylaxis against migraine participated in a double blind placebo controlled trial of the herb: eight patients received capsules containing freeze dried feverfew powder and nine placebo. Those who received placebo had a significant increase in the frequency and severity of headache, nausea, and vomiting with the emergence of untoward effects during the early months of treatment. The group given capsules of feverfew showed no change in the frequency or severity of symptoms of migraine. This provides evidence that feverfew taken prophylactically prevents attacks of migraine, and confirmatory studies are now indicated, preferably with a formulation controlled for sesquiterpene lactone content, in migraine sufferers who have never treated themselves with this herb.
The therapeutic activity of feverfew on migraines and epilepsy may be due to its GABA-benzodiazepine modulatory effects.

GreenMedInfo Summary

Abstract Title: Bioassay-guided isolation of apigenin with GABA-benzodiazepine activity from Tanacetum parthenium.


Abstract

Extracts of Tanacetum parthenium are used in the prophylactic treatment of migraine and have also been used in Danish folk medicine for the treatment of epilepsy. An ethanol extract of T. parthenium showed high affinity for the GABA(A)-benzodiazepine site. An ethanol extract of T. parthenium was fractionated by VLC on silica and preparative C18 HPLC. Each step was monitored with the GABA(A)-benzodiazepine bioassay. The fractionation led to the isolation of apigenin, which may be responsible for CNS-effects of T. parthenium extracts.
The efficacy and safety of feverfew (Tanacetum parthenium L.): An update of a systematic review.

Ernst E, Pittler MH. Public Health Nutr. 2000 Dec;3(4A):509-14. Department of Complementary Medicine, School of Postgraduate Medicine and Health Science, University of Exeter, UK. e.ernst@exeter.ac.uk

Abstract

OBJECTIVE:
Feverfew (Tanacetum parthenium L.) is a popular herbal remedy often advocated for the prevention of migraine. The aims of this systematic review are to update the evidence from rigorous clinical trials for or against the efficacy of feverfew for migraine prevention and to provide a safety profile of this herbal remedy.

DESIGN:
Literature searches were performed using the following databases: Medline, Embase, Biosis, CISCOM and the Cochrane Library (all from their inception to December 1999). Only randomized, placebo-controlled, double-blind trials of feverfew mono-preparations for the prevention of migraine in human subjects were included. All articles were read by two independent reviewers. Data were extracted in a pre-defined, standardized fashion. The methodological quality of the trials was evaluated by the Jadad score. For the assessment of safety issues, major reference texts were also consulted.

RESULTS:
Six trials met the inclusion/exclusion criteria. The majority favour feverfew over placebo. Yet important caveats exist. The data also suggest that feverfew is associated with only mild and transient adverse effects and few other safety concerns.

CONCLUSIONS:
Feverfew is likely to be effective in the prevention of migraine. There are no major safety problems.
Gene response of human monocytic cells for the detection of anti-migraine activity of feverfew extracts.

Chen CF, Leung AY. Can J Physiol Pharmacol. 2007 Nov;85(11):1108-15. Source - Department of Genetics and Biochemistry, Jordan Hall 100, Clemson University, Clemson, SC 29634, USA. cchen@clemson.edu

Abstract

The herb feverfew is a folk remedy for various conditions, including inflammation, fever, psoriasis, rheumatism, and asthma. Like many herbal medicines, feverfew's mechanisms of action in the human body are largely unknown and its active ingredients remain elusive. Very often, different extraction methods of herb material produce different physical and biochemical properties and variation in clinical efficacy. We identified 3 major methods of extraction for feverfew aerial parts and used microarray technology to test the hypothesis that extracts produced by different methods elicit different gene expression profiles. We have identified approximately 200 genes that are consistently regulated by the 2 presumptive active anti-migraine feverfew extracts but not associated with the inactive extract. Our results suggest that the presumptive active feverfew extracts potently stimulate more genes in human cells than the inactive extracts. We also identified several genes as unique signatures for these active extracts. All 3 feverfew extracts exhibited similar blockades on lipopolysaccharide-mediated TNF-alpha (tumor necrosis factor alpha) release, implicating that TNF-alpha is not responsible for the differences in the effects of the 3 feverfew extracts in human cells. In contrast, the active extracts more effectively suppressed CCL2 (also known as monocyte chemoattractant protein 1, MCP-1) than the inactive extracts, suggesting that CCL2 is a potential cellular target for feverfew's anti-migraine effects.
Application of NFkappaB inhibitor for arthritis.

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Abstract

Recent progress in DNA technologies has provided the strategies to regulate the transcription of disease-related genes in vivo using antisense oligodeoxynucleotide (ODN). Transfection of cis-element double-stranded oligodeoxynucleotides (decoy ODNs) has been reported as a new therapeutic tool of anti-gene strategies for gene therapy. In the field of arthritis, decoy ODNs strategies have been significant therapeutic potential. In vitro studies demonstrated that the inhibitory effect on inflammatory cytokines and matrix The concept of regulation the disease related gene expression at the level of transcriptional factor may be more therapeutic effects compared with monotherapy in arthritis. Injection of NFkappaB decoy ODN into the affected joint resulted in marked suppression of joint destruction in CIA models. metalloproteinase production from stimulated synovial cells derived from rheumatoid arthritis patients. NFkappaB decoy ODN inhibited induction of osteoclasts and bone resorption ability. Parthenolide is one of the main sesquiterpene lactones responsible for the bioactivities of feverfew and recently reported to inhibit NFkappaB activation. Parthenolide has ameliorated the severity of joint destruction in experimental animal model. Based upon these findings, NFkappaB may be one of important therapeutic target for arthritis.
Inhibition of 5-lipoxygenase and cyclo-oxygenase in leukocytes by feverfew. Involvement of sesquiterpene lactones and other components.


Abstract

Leaves or infusions of feverfew, Tanacetum parthenium, have long been used as a folk remedy for fever, arthritis and migraine, and derived products are widely available in U.K. health food shops. Previous reports have suggested interactions with arachidonate metabolism. Crude chloroform extracts of fresh feverfew leaves (rich in sesquiterpene lactones) and of commercially available powdered leaves (lactone-free) produced dose-dependent inhibition of the generation of thromboxane B2 (TXB2) and leukotriene B4 (LTB4) by ionophore- and chemoattractant-stimulated rat peritoneal leukocytes and human polymorphonuclear leukocytes. Approximate IC50 values were in the range 5-50 micrograms/mL, and inhibition of TXB2 and LTB4 occurred in parallel. Isolated lactones (parthenolide, epoxyartemisin) treated with cysteine (to neutralize reactive alpha-methylene butyrolactone functions of the sesquiterpenes). Inhibition of eicosanoid generation appeared to be irreversible but not time-dependent. We conclude that feverfew contains a complex mixture of sesquiterpene lactone and non-sesquiterpene lactone inhibitors of eicosanoid synthesis of high potency, and that these biochemical actions may be relevant to the claimed therapeutic actions of the herb.
Magnesium: Anti-inflammatory and Analgesic Studies

- Relation Between Serum Magnesium Level and Migraine Attacks
  Oral Magnesium Oxide Prophylaxis of Frequent Migrainous Headache in Children: a Randomized, Double-blind, Placebo Controlled Trial

- Prophylaxis of Migraine with Oral Magnesium: Results from a Prospective, Multi-Center, Placebo-Controlled and Double-Blind Randomized Study.

- Magnesium in Migraine: Results of a Multicenter Pilot Study
- Magnesium in the Prophylaxis of Primary Headache and Other Periodic Disorders in Children

- Dietary Magnesium Intake is Inversely Associated with Serum C-Reactive Protein Levels: Meta-Analysis and Systematic Review

- A Double-Blinded Randomised Controlled Study of the Value of Sequential Intravenous and Oral Magnesium Therapy in Patients with Chronic Low Back Pain with a Neuropathic Component.
MAGNESIUM: ANTI-INFLAMMATORY AND ANALGESIC STUDIES

A major mechanism of pain is the excessive stimulation of a brain chemical called "NMDA." The few medications that help decrease and balance this pain-carrying neurotransmitter have the downside of causing significant side effects. Magnesium seems to settle down NMDA without the toxicity. Magnesium deficiency can be a major amplifier of pain. Because of food processing, most people are magnesium deficient. If you have pain, taking magnesium each day can start to decrease these deficiencies as well as the pain, after just several weeks.

Relation between serum magnesium level and migraine attacks.


Abstract

OBJECTIVE:
The determination of serum magnesium levels in migraine.

METHODS:
In a case control study performed between January 2007 and December 2007 at Tabriz University of Medical Sciences, Tabriz, Iran, 140 migraine patients were enrolled and their level of serum magnesium was determined and the results were compared with 140 healthy people who did not have any headache, kidney, or gastrointestinal disorders, and no consumption of magnesium complements.
RESULTS:
Migraine patients (22 male, 118 female) with a mean age of 33.82+-10.31 and 140 healthy people (26 male, 114 female) with a mean age of (34.19+-9.95) were enrolled. Forty patients had aura and 100 patients did not have aura. The average serum magnesium level in the patient group (26.14+-4.3) was significantly lower than the control (31.09+-4.32) group (p=0.000). There was no significant difference between the mean level of serum magnesium in patients with migraine with aura and without aura, however, there was a significant linear relationship between the amount of serum magnesium and the frequency of headache.

CONCLUSION:
Serum magnesium in migraine patients was significantly lower than the normal population and related to the frequency of migraine attacks, supporting the use of magnesium in prevention and treatment of migraine.

Oral magnesium oxide prophylaxis of frequent migrainous headache in children: a randomized, double-blind, placebo-controlled trial.


Abstract

OBJECTIVE:
To assess whether, in children, oral magnesium oxide reduces migrainous headache frequency, severity, and associated features compared to placebo.

BACKGROUND:
There is no single, safe, widely well-tolerated, and effective prophylactic treatment for all children and adolescents with frequent migrainous headache.

DESIGN:
Randomized, double-blind, placebo-controlled, parallel-group trial.
METHODS:
This study was conducted between June 1997 and January 2000 using 7 selected Northern California Kaiser Permanente sites. We recruited children of ages 3 to 17 years who reported a 4-week history of at least weekly, moderate-to-severe headache with a throbbing or pulsatile quality, associated anorexia/nausea, vomiting, photophobia, sonophobia, or relief with sleep, but no fever or evidence of infection. Subjects were randomly assigned to receive either magnesium oxide (9 mg/kg per day by mouth divided 3 times a day with food) (n = 58) or matching placebo (n = 60) for 16 weeks. The number of headache days (days with at least one headache) during each of eight 2-week intervals was chosen to be the primary outcome variable.

RESULTS:
Of those enrolled, 86 (73%) completed the study (42 received magnesium oxide and 44 placebo); 74 of 192 eligible subjects declined to participate. Baseline information on demographic factors, health status, and headache history was similar comparing the 2 groups. By intention-to-treat analysis, we found a statistically significant decrease over time in headache frequency in the magnesium oxide group (P = .0037) but not in the placebo group (P = .086), although the slopes of these 2 lines were not statistically significantly different from each other (P = .88). The group treated with magnesium oxide had significantly lower headache severity (P = .0029) relative to the placebo group.

CONCLUSIONS:
This study does not unequivocally determine whether oral magnesium oxide is or is not superior to placebo in preventing frequent migrainous headache in children, but treatment with the active agent did lead to a significant reduction in headache days. Larger trials involving this safe, appealing complementary therapy are needed.
Prophylaxis of migraine with oral magnesium: results from a prospective, multi-center, placebo-controlled and double-blind randomized study.


Abstract

In order to evaluate the prophylactic effect of oral magnesium, 81 patients aged 18-65 years with migraine according to the International Headache Society (IHS) criteria (mean attack frequency 3.6 per month) were examined. After a prospective baseline period of 4 weeks they received oral 600 mg (24 mmol) magnesium (trimagnesium dicitrate) daily for 12 weeks or placebo. In weeks 9-12 the attack frequency was reduced by 41.6% in the magnesium group and by 15.8% in the placebo group compared to the baseline (p < 0.05). The number of days with migraine and the drug consumption for symptomatic treatment per patient also decreased significantly in the magnesium group. Duration and intensity of the attacks and the drug consumption per attack also tended to decrease compared to placebo but failed to be significant. Adverse events were diarrhea (18.6%) and gastric irritation (4.7%). High-dose oral magnesium appears to be effective in migraine prophylaxis.
Magnesium in migraine. Results of a multicenter pilot study.


Abstract

BACKGROUND:
 Numerous experiments and clinical observations have credited magnesium with a positive influence on the incidence of migraine attacks.

METHODS:
 With the aim of testing this hypothesis, a doubleblind, cross-over multicenter pilot study was initiated. The study contained 43 migraine patients who met the criteria of the international Headache Society.

INTERVENTIONS:
 Administration of 600 mg magnesium/day in the form of trimagnesium dieltrate for prophylaxis.

RESULTS:
 Under this medication, a significant reduction in the incidence of migraine attacks was observed. Although the level of effectiveness of the regimen does not appear to be as high as that of presently approved migraine prophylactic substances, a very low rate of side effects can be expected.

CONCLUSION:
 The working hypothesis to the effect that magnesium may be useful in the prevention of migraine attacks has been confirmed by the pilot study. Further studies aimed at determining dosage and enabling a further differentiation of patient material are in preparation.
Magnesium in the prophylaxis of primary headache and other periodic disorders in children.

Castelli S\textsuperscript{1}, Meossi C, Domenici R, Fontana F, Stefani G.

Abstract

Migraine has been recently defined a "central neuronal hyperexcitability state", maybe magnesium-dependent, and magnesium has been occasionally employed in the therapy of adult migraine. The Authors, on the basis of their personal experience (previous electromyographic studies), consider childhood migraine and periodic syndrome as a clinical equivalent of spasmophilia, in which an intracellular deficit of magnesium has been demonstrated, and have employed a magnesium salt in the prophylaxis of childhood migraine and migraine equivalents. 40 children with periodic syndrome (17 M and 23 F, aged 10.4 +/- 2.9 years) have been treated with magnesium pidolate, with doses ranging from 1.5 g/die to 4.5 g/die (corresponding to 122-366 mg Mg++): 25 of them presented migraine as the main symptom, 12 recurrent abdominal pain, 3 fever of unknown origin, along with many other periodic symptoms. The first control visits have been done at 1 month, clinical follow-up lasted a mean period of 6.1 months. Therapy was stopped at 1 month visit if ineffective (of some other drug was added); otherwise, magnesium therapy was continued with the same dosage for another month, then gradually reduced. Clinical response was considered good if crises ceased completely or their frequency was reduced to less than 33%; partial if reduced to less than 67% of previous incidence; absent if only slightly or not at all reduced. Clinical response was good in 72.5% of cases at 1 month, in 77.5% later; partial in 12.5% and 10%; absent in 15% and 12.5% respectively. No side effects were observed. The compliance of children and their families was complete.
Dietary magnesium intake is inversely associated with serum C-reactive protein levels: meta-analysis and systematic review.


Abstract

Background/objectives: The aim of this study was to quantitatively summarize the association of dietary magnesium (Mg) intake with serum C-reactive protein (CRP) levels in the general population. Subjects/methods: Observational and experimental studies through February 2013 were reviewed in PubMed and EMBASE. Additional information was retrieved through Google or hand search of related reference lists. The main outcome is either adjusted geometric mean of CRP or odds ratio (OR) of having serum CRP $\geq$ 3 mg/l. Meta-regression was used to determine the linear association of dietary Mg intake and adjusted geometric means of CRP levels. A fixed-effects model was used to pool ORs of interest, comparing those in the lowest with those in the highest group of dietary Mg intake. Results: A data set derived from seven cross-sectional studies including 32,918 participants was quantitatively assessed. A weighted inverse association between Mg intake and serum CRP levels was observed ($\beta$-coefficient: -0.0028; 95% confidence interval (CI), -0.0043 to -0.0013; $P_{\text{trend}}=0.001$) from four cross-sectional studies. The pooled OR (95% CI) of having CRP $\geq$ 3 mg/l was 1.49 (1.18-1.89) on comparing the lowest to the highest group of Mg intake from three studies with the data available. Qualitative assessment among five intervention studies also showed a potential beneficial effect of Mg intake on serum CRP levels. Conclusions: This meta-analysis and systematic review indicates that dietary Mg intake is significantly and inversely associated with serum CRP levels. The potential beneficial effect of Mg intake on chronic diseases may be, at least in part, explained by inhibiting inflammation. European Journal of Clinical Nutrition advance online publication. 12 February 2014; doi:10.1038/ejcn.2014.7.
A double-blinded randomised controlled study of the value of sequential intravenous and oral magnesium therapy in patients with chronic low back pain with a neuropathic component.


Abstract

Persistent mechanical irritation of the nerve root sets up a series of events mediating sensitisation of the dorsal roots and dorsal horns in the spinal cord. Current evidence supports the role of magnesium in blocking central sensitisation through its effect on N-methyl-d-aspartate receptors. We studied the role of sequential intravenous and oral magnesium infusion in patients with chronic low back pain with a neuropathic component. We recruited a cohort of 80 patients with chronic low back pain with a Leeds Assessment of Neuropathic Signs and Symptoms pain scale score ≥ 12, who were receiving a physical therapy programme. All patients were treated with anticonvulsants, antidepressants and simple analgesics; in addition 40 patients received placebo for 6 weeks (control group), while the other 40 patients received an intravenous magnesium infusion for 2 weeks followed by oral magnesium capsules for another 4 weeks (magnesium group). Patients were asked to rate their pain using a numerical rating scale. Lumbar spine range of motion was also determined using a long-arm goniometer. In the magnesium group, the patients' numerical rating scales revealed a significant reduction in pain intensity. The mean (SD) pre-treatment value was 7.5 (2.2) compared with 4.7 (1.8) at 6 months (p = 0.034). The reduction in pain intensity was accompanied by significant improvement in lumbar spine range of motion during the follow-up period. The mean (SD) values of flexion, extension and lateral flexion movements before treatment and at 6-month follow up were 22.2 (8.4) vs 34.7 (11.5) (p = 0.018), 11.8 (3.4) vs 16.9 (3.5) (p = 0.039), 11.4 (3.6) vs 17.2 (4.4) (p = 0.035), respectively. Our findings show that a 2-week intravenous magnesium infusion followed by 4 weeks of oral magnesium supplementation can reduce pain intensity and improve lumbar spine mobility during a 6-month period in patients with refractory chronic low back pain with a neuropathic component.